DOCKET NO.: CEPH-2313 (CP188-C) PATENT

Application No.: 10/685,923

Office Action Dated: April 27, 2004

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1. (original) A compound having the Formula I:

$$Q \longrightarrow (Aaa)_{\overline{n}} \longrightarrow (N \longrightarrow M \longrightarrow C \longrightarrow)_{q} \longrightarrow NH \longrightarrow C \longrightarrow Z$$

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wherein:

Q has the formula G-B- $(CHR^4)_V$ where R^4 is independently H or alkyl having from 1 to 4 carbons;

v is 0, 1, or 2;

B is selected from the group consisting of C(=0), OC(=0), S(=0)_m, CH₂, a bond, NR⁵C(=0), S (=0) _m-A-C (=0), and C(=0)-A-C(=0), where R⁵ is H or lower alkyl;

m is 0, 1, or 2;

A is lower alkylene or cycloalkylene, optionally substituted with one or more halogen atoms, aryl, or heteroaryl groups;

M is a carbon atom;

G is selected from the group consisting of H, a blocking group, lower alkyl, lower alkenyl, aryl having from about 6 to about 14 carbons, heterocyclyl having from about 5 to about 14 ring atoms, heterocycloalkyl having from about 5 to about 14 ring atoms, arylalkyl having from about 7 to about 15 carbons, heteroarylalkyl, and arylheteroalkyl wherein the aryl portion can be unfused or fused with the heteroalkyl ring, said alkyl, aryl heterocyclyl, heterocycloalkyl, arylalkyl, heteroarylalkyl, and arylheteroalkyl groups being optionally substituted with one or more J groups;

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J is selected from the group consisting of halogen, CN, nitro, lower alkyl, cycloalkyl, heterocycloalkyl, heteroalkyl, halogenated alkyl, aryloxyalkyl, alkylthio, alkylsulfonyl, aryl, heteroaryl, arylalkyl, arylalkyloxy, arylsulfonyl, heteroarylsulfonyl, alkoxycarbonyl, alkoxyalkyl, acyl, alkoxy, hydroxy, carboxy, hydroxyalkyl, amino, alkylamino, and aminoalkyl, said amino group or said amino group of said aminoalkyl or alkylamino group being optionally substituted with an acyl group, an alkoxy group, or with 1 to 3 aryl, lower alkyl, cycloalkyl, or alkoxyalkyl groups; and said aryl, heteroaryl, heterocycloalkyl, and heteroalkyl groups being further optionally substituted by a J group;

each Aaa is independently an amino acid which optionally contains one or more blocking groups;

n is 0, 1, 2, or 3;

R¹ and R² are independently selected from the group consisting of H, alkyl having from one to about 6 carbons, arylalkyl having from about 7 to about 15 carbons, heteroalkyl in which the ring contains from about 5 to about 14 ring atoms, heteroarylalkyl in which the heteroaryl ring contains from about 5 to about 14 ring atoms, alkoxyalkyl, a side chain of a naturally occurring amino acid in the R or S configuration, and (CH₂)_PNH-L, said alkyl, arylalkyl, heteroalkyl, heteroarylalkyl, and alkoxyalkyl groups being optionally substituted with one or more J groups;

p is 0, 1, 2, or 3;

L is selected from the group consisting of alkoxycarbonyl having from 2 to about 7 carbons, arylalkoxycarbonyl in which the arylalkoxy group contains about 7 to about 15 carbons, and $S(=0)_2R^6$;

R⁶ is selected from the group consisting of lower alkyl, and aryl having from about 6 to about 14 carbons;

 R^3 is selected from the group consisting of H, alkyl having from one to about 6 carbons, arylalkyl having from about 7 to about 15 carbons, heteroalkyl in which the ring contains from about 5 to about 14 ring atoms, heteroarylalkyl in which the heteroaryl ring contains from about 5 to about 14 ring atoms, alkoxyalkyl, a side chain of a naturally occurring amino acid in the R or S configuration, $(CH_2)_PNH-L$, $C(=0)R^7$, $S(=0)_2R^7$, a blocking group, and when combined with the

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carbon atom to which R¹ is attached an alkylene group having from 2 to 5 carbons, said alkylene group being optionally substituted with a group selected from the group consisting of aryl, azide, CN, a protected amino group, and OS0₂-aryl, said alkyl, arylalkyl, heteroalkyl, heteroarylalkyl, and alkoxyalkyl groups being optionally substituted with one or more J groups;

R⁷ is selected from the group consisting of aryl having from about 6 to about 14 carbons, heteroaryl having from about 5 to about 14 ring atoms, arylalkyl having from about 7 to about 15 carbons, alkyl having from 1 to about 10 carbons, said aryl, heteroaryl, arylalkyl and alkyl groups being optionally substituted with one or more J groups, heteroalkyl having from 2 to about 7 carbons, alkoxy having from about 1 to about 10 carbons, and amino optionally substituted with 1 or more alkyl groups;

q is 0 or 1;

Z is selected from the group consisting of $C(=0)C(=0)NH-X-A^1-K$ and

$$- \begin{bmatrix} 0 & 0 \\ 0 & H \end{bmatrix}$$

X is a bond or -0-;

 A^1 is the same as A;

K is selected from the group consisting of $N(R^{10})Y$,

D is a fused aryl or heteroaryl group;

R¹¹ is selected from the group consisting of alkoxy, aryloxy, and NHR¹²;

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R¹² is selected from the group consisting of H, alkyl, aryl, and heteroaryl, said alkyl, aryl or heteroaryl groups being optionally substituted with one or more J groups;

Y is selected from the group consisting of $SO_{:}R^{8}$, 10 C(=0)NHR⁹, C(=S)NHR⁹, C(=NCN)R¹¹, C (=NC (=0) NHR¹⁰) R¹¹, and C0₂R⁸;

R⁸ is selected from the group consisting of alkyl, alkoxy, aryl, and heterocyclyl, said alkyl, alkoxy, aryl, or heterocyclyl groups being optionally substituted with one or more J groups;

R⁹ is selected from the group consisting of H, alkyl, aryl, and heteroaryl, said alkyl, aryl, or heteroaryl groups being optionally substituted with one or more J groups;

or an R⁹ alkyl group may be combined with an A¹ alkylene group to form a N-containing heterocyclic 5- or 6-membered ring;

R¹⁰ is selected from the group consisting of H and lower alkyl;

or in the moiety S0₂N(R⁹)R¹⁰, R⁹ and R¹⁰ may be combined together with the N atom to which they are attached to form a N-containing heterocyclic 5- or 6-membered ring;

or where A¹ is an alkylene group, and K is N(R¹⁰)Y wherein R¹⁰ is alkyl, said R¹⁰ alkyl group may be combined with said A¹ alkylene group to form a N-containing heterocyclic 5- or 6-membered ring;

or a pharmaceutically acceptable salt thereof.

- 2. (original) The compound of claim 1 wherein n and v are each 0, q is 1, B is a bond, and G is H.
- 3. (original) The compound of claim 1 wherein R¹ is the side chain of a naturally-occurring amino acid.
- 4. (original) The compound of claim 1 wherein R^3 is $-S(=0)_2R^7$.
- 5. (original) The compound of claim 1 wherein R² is benzyl or alkoxyalkyl.

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6. (original) The compound of claim 1 wherein X is a bond, and Y is $S0_2R^8$.

7. (original) The compound of claim 1 wherein A¹ is -CH₂-CH₂-, -CH₂-CH(CH₃)-, or - (CH₃)CH-CH₂-.

- 8. (presently amended) The he compound of claim 1 wherein R¹ is a serine side chain, which is optionally capped with a benzyl group.
- 9. (original) The compound of claim 8 wherein M is a carbon atom in the D configuration.
- 10. (original) The compound of claim 1 wherein R² is benzyl, R⁷ is methyl, and R⁸ is substituted phenyl, unsubstituted phenyl, substituted heteroaryl, or unsubstituted heteroaryl.
- 11. (original) The compound of claim 1 wherein R⁸ is aryl, aryl substituted with amino, aryl substituted with heterocyclomethyl, heteroaryl, alkyl substituted with heteroaryl, or heteroaryl substituted with alkylthio, haloalkyl, alkyl, phenylsulfonyl, halogen, aminophenyl, amino, or dialkylaminoalkyl.
- 12. (original) The compound of claim 1 wherein n and v are each 0, q is 1, R^1 is the side chain of an amino acid in the D- or L-configuration, R^3 is $S(=0)_2R^7$, G is H, B is a bond, R^2 is benzyl or alkoxyalkyl, X is a bond, and Y is $S0_2R^8$.

13. (cancelled)

14. (original) The compound of claim 1 wherein R¹ is a serine side chain in the D-configuration in which the hydroxyl group is capped with benzyl, R² is benzyl, R⁷ is methyl, and R⁸ is substituted or unsubstituted phenyl or substituted or unsubstituted heteroaryl.

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15. (presently amended) The compound of claim 1 wherein $Ri-R_4$ R_1-R_4 , B, G, Aaa, X, A¹, Y, n, q and v are selected in accordance with Tables 2 and 3.

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Claims 16 to 19 (cancelled)

20. (original) The compound of claim 1 having the formula:

$$\begin{array}{c} W \\ N \\ H \end{array} \begin{array}{c} Ph \\ O \\ N \\ H \end{array} \begin{array}{c} R \\ R \end{array}$$

wherein W and R are independently selected from the group of substituents shown in Table 4.

21. (original) The compound of claim 20 wherein W and R are selected in accordance with Table 4.

Claims 22 to 23 (cancelled)

- 24. (original) The compound of claim 1 wherein n, v and q are each 0; B is (C=0); and G is phenyl or lower alkyl, said phenyl or lower alkyl groups being optionally substituted with one or more J groups.
- 25. (original) A composition for inhibiting a serine protease or a cysteine protease comprising a compound of claim 1 and a pharmaceutically acceptable carrier.
- 26. (*original*) A method for inhibiting a serine protease or a cysteine protease comprising contacting a protease selected from the group consisting of serine proteases and cysteine proteases with an inhibitory amount of a compound of claim 1.